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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,335	12/21/2001	Sivaram Pillarisetti	18631-0121 (45115-264494)	1157

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/626,335	PILLARISETTI et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 12/6/04.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-6, 8-14, 16-34 is/are pending in the application.

Of the above claim(s) 8-9, 16-26 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-6, 10-14, 27-34 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

The claims pending are 1-6, 8-14 and 16-34.

Applicant's election with traverse of Group I (claims 1-6, 10-14 and 27-34 in the reply filed on 12/06/04 is acknowledged. The traversal is on the ground(s) that examining all groups would not constitute a serious burden. This is not found persuasive because Applicant has merely presented a conclusonary statement regarding the burden. To the contrary, the examiner considers a search for the compound and its use in treatment burdensome because, firstly, if one is screening a compound (e.g. from a library) the compound must have already been known. The assay merely characterizes an inherent property of a known compound and does not impart patentability to the compound per se. Secondly, the compound has not been described (applicant has not described one compound; designating test compounds as A1-A7 discloses nothing); thus the examiner has no idea as to where the searches for the compound and its use in treatment should be conducted. The examiner notes that TNF alpha is the elected species of secreted determinant; however, other species will be examined in any references submitted in the IDS.

The requirement is still deemed proper and is therefore made FINAL.

The disclosure is objected to because of the following informalities: At page 3, lines 24-26, and at numerous following locations, a black dot appears where a Greek letter is intended.

Appropriate correction is required.

Except for the above objection to the specification, the examiner will make further reference to the specification in terms of para. number, as set forth in Pre-grant publication 2002/0086282.

Claims 4, 10, 13 and 24 are objected to because of the following informalities: In claim 4 a comma is believed intended after "emulsion" and after "hormone". In claim 10, last line "from cells" is surplusage. In claim 13 a comma is considered intended after "hormone". In claim 24 a comma is believed intended after "arthritis". Appropriate correction is required.

Claims 1-6, 10-14 and 27-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 1 "activity" is unclear as to what kind of activity is intended; at line 4, "stimulatory agent" is unclear as to what kind of cell activity or function is intended to be stimulated. In step c) (lines 5-8), it is not clear if the secreted determinant is obtained from the all culture or from another source. In step d) (lines 8-9), no conclusion is drawn from the "comparing" that relates to the goal set forth in the preamble.

Like considerations apply to steps c) – d) of claim 10, and to steps b) – d) of claim 27.

Claims 4, 13 and 28 have an improper Markush group; a "chemical element" cannot properly be considered as a species of the genus of "compounds". Also, a "compound" (third member) is the same as the genus. In addition, a "mixture" cannot

be considered as a species of the genus of "compounds"; applicant's definition of "compound" at para. [0016] is repugnant.

In claim 14, "the stimulatory agent" lacks antecedent basis.

Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The assay of claim 10 does not enable the detecting of any composition that "affects glycated protein accumulation" as stated in the preamble.

The assay as claimed in step c) measures a secreted determinant which has been disclosed a group of endothelial cytokines, the secretion of which is induced by AGE or glycated proteins. See para. [0007], [0013], [0015], and [0023], for example. These cytokines and other recited determinants mediate inflammation that results from the accumulation of AGE and glycated proteins. A such the assay does not identify the detecting of the effect of any composition upon "glycated protein accumulation". Applicant has disclosed that the formation of Amadori adducts and further enzymatic or non-enzymatic rearrangements incur the accumulation of AGE and glycated proteins. See para. [0003], and [0018]. Since step c) of claim 10 does not determine the production of any product resulting from such enzymatic or non-enzymatic processes, claim 10 does not enable one to any composition that "affects glycated protein accumulation."

Note that the only proper correction to claim 10 would be an amendment that changes the purpose set forth in the preamble to be consistent with what the claimed process steps enable. The examiner can only search and examine what is set forth in the body of the claim. Any changes in the body, to render the steps consistent with the presently recited preamble will result in withdrawal of claim 10 and its dependents, as non-elected by original presentation.

Claims 1-6, 10-14 and 27-34 are rejected under 35 U.S.C. 112, first paragraph, as contain(ing) subject matter, which was not described in the specification in such a way as to enable one skilled in the relevant art to make and/or use the claimed invention. Step c) of each of claims 1, 10 and 27 has not been enabled for all of the recited "secreted determinants of inflammation".

Specifically the examiner does not consider that each of the recited determinants can be properly considered as "secreted". For example, the Markush group members recited as "adhesion molecules", "selectins", and "V-CAM-1" are not "secreted" but, rather, are expressed on the cell surface. See Sengoelge et al (ref AB), who measured adhesion molecules, such as VCAM-1 and ICAM-1, and E-selectin on the cell surface, rather than in the culture medium, following stimulation with glycated HSA. Since these molecular determinants are not "secreted", the invention cannot be practiced for these embodiments. The examiner lacks sufficient familiarity with the art to known whether other members recited are likewise not "secreted". Applicant is required to cancel recitations of all determinant members of the Markush Group, which are not "secreted".

For example, Examiner considers that NF-kB is intracelluitarly expressed and not "secreted".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-6, 10-11, 13-14 and 27-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bian et al (Curr Eye Res, 12, 439,1997).

Bian et al teach when HCKs (corresponding to the instant "cells") are incubated with G-HSA (corresponding to instant "stimulatory agent") they secrete IL-8 and MCP-1 (the latter corresponding to a recited "secreted determinant"). See page 67, col. 1 and Fig. 1. This culturing corresponds to what is accomplished with the instant "second cello culture". Bian et al also treat a like cell culture by adding glucose (corresponding to instant "compound") prior to stimulation with the G-HSA. They compare IL-8 and MCP-I secretion in cultures with and without addition of glucose. See para. spanning pages 67-68 and Table 2. They show that addition of glucose increases the secretion of IL-8 and MCP-1.

Applicant's claim 1 is so vague as to what is meant by "activity" (preamble) and as to what is to be concluded from the "comparing" (step a)) that anticipatation is proper.

Applicant's claim 10 is deemed to have nonenabled goal recited in the preamble (112, first supra). Since its steps are essentially the same as in clam 1 and since no conclusion is drawn from the "comparing (step d)), anticipation is proper.

For like reasons claim 27 is properly, rejected.

Claim 29 is included, since Bian et al teach that diabetic patients may be more prone to HCK-medicated keratitis. See page 70, col. 8.

Claims 1-2, 4, 10-11, 13, 27-29 and 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Yan et al (PNAS, 94, 5296,1997).

Yan et al teach that when human neuroblastoma cells (corresponding to instant "cells") are incubated with beta amyloid peptide (A. beta., corresponding to the instant "stimulatory agent") they secret M-CSF (corresponding to instant "secreted determinant"). See page 5298, col. 1; this culturing corresponds to what is accomplished with the instant "second cell culture". Yan et al also treat like cell cultures with the addition of cyclohexamide, N-acetylcysteine, or anti-RAGE (These three additives correspond to the instant "compound") one hour prior to the addition of the stimulating A. beta. See page 5298, col. 1 and legend to Figs 2A-2B. They show that these three additives inhibit the secretion of M-CSF by the neurolblastomice cells.

As noted supra regarding Bian et al, applicant's claims are so vague as to what is meant by "activity" in the preamble and as to what is concluded from step d) that anticipation is properly stated.

Claim 29 is rejected since A. beta. is related to Alzheimer's disease.

The following reference is cited as of interest:

Medford et al (5,846,959) teach aspects of the instant invention by measuring the expression of VCAM-1 on the cell surface, following treatment with a stimulatory agent such as TNF, alpha, or IL-1. beta. Various antioxidants – inhibit this expression of VCAM-1. See Figs. 13 a-b and 14. See col. 7, lines 4^{+} and col. 23, line 61 – col. 24, line 34. Since VCAM-1 is on the cell surface and not "secreted" as required by instant claims 1, 10 and 27, step (C) of each; the reference is not cited against the claims. However, should the claims be amended to encompass cell surface expression of the "determinant", or should applicant indicate on the record that "secreted" encompasses being bound to the cell surface, then the examiner may cite Medford et al in a final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/LR
February 16, 2005